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09/750,373	12/28/2000	Peter Lind	008USPHRM300	7317

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EXAMINER
LANDSMAN, ROBERT S

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1647	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/750,373	Applicant(s) LIND ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10,12-25 and 29-89* is/are pending in the application.

4a) Of the above claim(s) *34-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,12-25 and 29-33* is/are rejected.

7)☒ Claim(s) *9,10,12-24 and 29-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Formal Matters

A. Amendment A, filed 7/24/03, has been entered into the record.

B. Claims 1-89 were pending in the application. In Amendment A, Applicants cancelled claims 2-6, 11 and 26-28. Claims 34-89 have been withdrawn as being drawn to a non-elected invention. Therefore, claims 1, 7-10, 12-25 and 29-33 are the subject of this Office Action.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Title

A. The objection to the title has been withdrawn in view of Applicants' amendments to remove the term "novel" and to clearly indicate that the invention to which the claims are directed is polynucleotides and not receptors themselves.

3. Claim Objections

A. The objection to claims 1, 7-10, 12-25 and 29-33 has been withdrawn in view of Applicants' amendment to the claims to remove non-elected subject matter (i.e. SEQ ID NOs).

B. The objection to claims 1, 7-10, 12-25 and 29-33 has been withdrawn in view of Applicants' amendment to the claims to remove the term "nGPCR-x."

C. The objection to claim 24 has been withdrawn in view of Applicants' amendment to the claim to insert the word "said" between "wherein" and "mammalian cell."

D. Claims 9, 10, 12-24 and 30-33 are objected to since claim 9 should be amended to recite "the nucleic acid molecule" instead of "a nucleic acid molecule" and claim 16 should be amended to recite "the expression vector" instead of "an expression vector." Claims 10, 12-15, 17-24 and 30-33 are also objected to since they depend from claims 9 or 16.

E. Claims 10 and 31-33 are objected to since they depend from claims rejected in paragraph B of the below rejection under 35 USC 112, first paragraph regarding enablement, paragraph A in the below rejection under 35 USC 112, first paragraph, written description, and paragraph A under 35 USC 102, but themselves are not rejected since the term "99% homology" is not pertinent in these claims since these claims recite entire known coding regions (i.e. 100% homology) of SEQ ID NOs disclosed in the specification.

F. Claim 29 is objected to since the syntax could be improved by replacing the phrase "any one of claims" with "claim." The phrase "any one of" is not required here since this implies selection of one item from a group of 3 or more. In this case, there are only 2 items to select from, claims 1 and 25.

G. Claims 30 and 31 are objected to since, even though it is understood in claims 9 and 10, from which claims 30 and 31 depend, respectively, that the expression vector is recombinant, there is no literal support for the antecedent basis of term "recombinant" in claims 30 or 31. Either claims 9 and 10 should be amended to include the term "recombinant" or this term should be removed from claims 30 and 31. In addition, the word "a" after the word "comprising" should be replaced with "the" in claims 30 and 31. Claims 32 and 33 are also objected to since they depend from claim 31.

4. Claim Rejections - 35 USC § 101

A. Claims 1, 7-10, 12-25 and 29-33 remain rejected under 35 USC 101 for the reasons already of record on pages 3-5 of the Office Action dated 2/6/03. Applicants argue that the claimed invention does have a credible, substantial and specific utility (i.e. real-word use) since it can be used to identify ligands and/or protein binding partners and that the polypeptides of the invention can be used to produce antibodies which can be used to localize the protein. Applicants further argue that being able to identify specific tissue types in the CNS can also aid in the identification of CNS defects and abnormalities. Applicants also argue that they need only provide a "substantial likelihood" of utility and that GPCRs have a well-established utility since many medically significant biological processes are mediated by signal transduction pathways involving G proteins and other second messengers and that GPCRs are recognized as important therapeutic targets for a wide range of diseases.

These arguments have been considered, but are not deemed persuasive. Hundreds of proteins, especially those of the G protein-coupled family of receptors, to which this protein is alleged to belong, can be used to produce antibodies, screen for ligands, or to identify diseases. Regarding using the protein

to identify ligands, this asserted utility is credible. However, it is not substantial, nor specific to the protein of the present invention. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure, for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial. Since numerous proteins can be used in these general assays, these uses are not specific to the protein of the invention.

Regarding the production of antibodies, this asserted utility is credible, but not specific nor substantial. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility. Regarding the identification of CNS disorders, or that GPCRs are used for therapeutic agents, these asserted utilities are credible, but neither specific nor substantial. The specification does not disclose any function, nor any dysfunction, associated with altered levels or forms of the polynucleotide or polypeptide of the claimed invention. Significant further experimentation would be required of the skilled artisan to identify a dysfunction or disease associated with the claimed polynucleotide or polypeptide. There is no disclosure, for example, of any symptoms associated with such a disease or dysfunction of the polypeptide. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not specific nor substantial. For the above reasons, Applicants have not demonstrated a "substantial likelihood" of utility, or that the invention has a "real-world" use.

Applicants further argue that all of the utilities described in the application are based on sound logic which is not inconsistent with the logic underlying the assertion that the polypeptides are useful and that the Office has provided no evidence that the logic is seriously flawed. These arguments have also been considered, but are also not deemed persuasive. Respectfully, the issue here is not that the logic regarding the asserted utility is flawed, since many proteins, in general, can be used to generate antibodies, to identify ligands, etc. The issue at hand is that Applicants have not provided a specific and substantial utility *for the protein of the present invention*. Applicants disclose in the specification that the claimed receptor is believed to be a G protein-coupled receptor. However, the basis that the receptor of the present invention is a 7 transmembrane, GPCR is not predictive of a use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This

further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

Applicants further argue that Brenner et al. (PNAS) teaches that the probability that the claimed polypeptide is related to the reference polypeptide is very high and that none of the reference cited by the Examiner contradicts Brenner's basic rule. Applicants' points regarding these references have been considered. Taken as a whole, these references show that prediction of novel proteins based on known homologous proteins is, at best, speculative. Even, *arguendo*, Brenner's rule was correct, Applicants have not identified to which protein(s) the protein of the present invention is related, nor, as argued on pages 3-5 of the Office Action dated 2/6/03, would this homology alone be sufficient to provide a utility of the present invention. If Applicants have support for specific identification of the protein, or polynucleotides, of the present invention as belonging to a specific subfamily of GPCRs, for example opioids or adrenergics, as well as specific assays further characterizing these proteins as such, they are required to point out exactly where in the specification this support can be found.

Applicants further argue In re Folkers. However, *In re Folkers* is concerned with the utility of a genus of *chemical compounds*, whereas the present invention is concerned with receptor *proteins*. Therefore, this issue is not relevant in this situation as follows. If Applicants were claiming that the protein of the present invention, or nucleic acids encoding these proteins, could be used as chemical compounds, then this argument may be relevant. However, whereas a genus of specific chemical compounds may have a utility, this is not analogous to a genus of receptors, in this case the entire superfamily of GPCRs, having a utility. For example, the LSD-like class of indoles may be used to better understand psychiatric disorders. However, this does not suggest that all compounds that have an indole nucleus will have the same or any utility. The same situation holds true for GPCRs. Whereas if Applicants have identified the GPCR of the present invention as belonging specifically to, for example, the opioid subfamily genus of GPCRs then, based on the art's knowledge of opioid pharmacology, the protein of the present invention would be expected to have a similar utility (analogous to the LSD compounds). However, this generalization cannot be extrapolated to a GPCR with a yet unknown function (e.g. indoles in general), as Applicants are attempting to do in the present situation. The GPCR family has too many variants to be considered a genus on the same level that Applicants are arguing *In re Folkers*.

Finally, Applicants bring to the Examiner's attention numerous patents claiming GPCRs with no natural substrate or specific biological significance. This argument has been considered, but is not persuasive. First, this application was properly examined under, and is consistent with, the current utility

guidelines, published 1/5/01, 66 FR 1092. Furthermore, all U.S. Patent are presumed valid, or would not have issued as U.S. Patents. It is believed that all pertinent arguments have been addressed.

Therefore, since the nucleic acid molecules of the invention do not possess a specific, substantial and credible asserted utility or a well established utility, the claimed expression vectors, host cells, compositions and methods of making the encoded protein, also do not possess utility.

5. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claims 1, 7-10, 12-25 and 29-33 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on page 5 of the Office Action dated 2/6/03 as well as for the reasons given in the above rejection under 35 USC 101. Applicants argue that the claimed invention is enabled because it has utility as argued previously. Applicants' arguments have been fully considered, but are not found to be persuasive for the reasons discussed above.

B. Furthermore, even if the present invention possessed utility under 35 USC 101, claims 1, 7-9, 12-24, 29 and 30 would still remain rejected under 35 USC 112, first paragraph, regarding the term "99% homologous" for the reasons already of record on pages 5-6 of the Office Action dated 2/6/03. The part of the rejection regarding the terms "fragments thereof" and "a portion" has been withdrawn in view of Applicants' amendments to remove these terms from the claims. Applicants argue that new claim 1 recites "99% homology" and, therefore, is not excessively broad and is easily understood by those of ordinary skill in the art. These arguments have been considered, but are not deemed persuasive. Nucleic acid molecules which encode a protein at least 99% homologous to SEQ ID NO:25 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:12, or to any polynucleotide encoding SEQ ID NO:25. Similarly, these proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:25. Furthermore, Applicants do not provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of the protein of SEQ ID NO:25. Therefore, the artisan would not know which residues to alter to the protein of SEQ ID NO:25 to make a functional protein which is less than 100% identical to SEQ ID NO:25. In addition, given this lack of guidance and working examples, it is not predictable to one of ordinary skill in the art how to make a functional protein which is less than 100% identical to that of SEQ ID NO:25.

In summary, there is a lack of guidance and working examples of proteins, or nucleic acid molecules which encode proteins, which are less than 100% identical to that of SEQ ID NO:25. Applicants have not provided guidance or working examples as to which residues are critical for protein function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make functional protein other that that of SEQ ID NO:25 leads the Examiner to maintain that undue experimentation is necessary to practice the invention as claimed. It is believed that all pertinent arguments have been addressed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1, 7-9, 12-24, 29 and 30 remain rejected under 35 USC 112, first paragraph, regarding the term "99% homologous" for the reasons already of record on page 7 of the Office Action dated 2/6/03. The part of the rejection regarding the terms "fragments thereof" and "a portion" has been withdrawn in view of Applicants' amendments to remove these terms from the claims. Applicants argue that new claim 1 recites "99% homology" and, therefore, is not excessively broad and is easily understood by those of ordinary skill in the art and that the artisan would understand that Applicants were in possession of the claimed invention when the application was filed. These arguments have been considered, but are not deemed persuasive. Nucleic acid molecules which encode a protein at least 99% homologous to SEQ ID NO:25 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:12, or to a polynucleotide encoding SEQ ID NO:25. Similarly, these proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:25. Furthermore, Applicants do not provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Applicants have not provided adequate written description of any protein other than that of SEQ ID NO:25, nor as to what critical residues are required to maintain the functional characteristics of the protein of SEQ ID NO:25. Therefore, the artisan would not know which residues to alter to the protein of SEQ ID NO:25 to make a functional protein which is less than 100% identical to SEQ ID NO:25. It is believed that all pertinent arguments have been addressed.

7: Claim Rejections - 35 USC § 102

A. Claims 1, 7-9, 12-24, 29 and 30 remain rejected under 35 USC 102 as being anticipated by Glucksmann et al. for the reasons already of record on page 8 of the Office Action dated 2/6/03. Applicants argue that Glucksmann et al. do not recite, nor suggest, a nucleic acid molecule that encodes a protein at least 99% identical to SEQ ID NO:25, or a nucleic acid molecule at least 99% identical to SEQ ID NO:12. Therefore, Glucksmann et al. fail to anticipate the claimed invention. These arguments have been considered, but are not deemed persuasive. First, the Examiner wishes to clarify that in the Office Action dated 2/6/03, the Examiner intended to state that Glucksmann et al. teach a nucleic acid molecule encoding *a protein* 98.8% identical to SEQ ID NO:25, not that the nucleic acid molecule of Glucksmann et al. was 98.8% identical to *the nucleic acid molecule* encoding SEQ ID NO:25. This, however, does not change the substance of the this rejection. This is further supported by reviewing Sequence Comparison A attached to the Office Action of 2/6/03, which clearly provides a nucleotide-protein comparison and not a nucleotide-nucleotide comparison.

Claim 1, as amended, recites that the protein is 99% identical to SEQ ID NO:25. This number is 2 significant digits. Glucksmann et al. teach a nucleic acid molecule (DNA) which is 98.8% identical to SEQ ID NO:25. This is 3 significant digits. Therefore, to maintain consistency between the percentages, 98.8 is rounded to 99. Therefore, Glucksmann et al. do, in fact, teach a nucleic acid molecule encoding a protein which is 99% identical to SEQ ID NO:25 of the present invention. As discussed in the rejection under 35 USC 102 on page 8 of Office Action of 2/6/03, one of ordinary skill in the art would immediately envision the RNA sequence, given the DNA sequence of Glucksmann et al. (see page 18, paragraph 0127). Also, as previously discussed, Glucksmann et al. also teach vectors, including plasmids, viral vectors such as adenovirus (page 16-17, paragraph 0115), promoters such as Simian Virus 40 (page 18, paragraph 0125), host cells such as E. coli and S.cerevisiae, S. frugiperda (i.e. sf9 cells) and mammalian cells such as African Green Monkey Kidney Cells (i.e. COS cells; page 18, paragraphs 0123, 0124, 0129). The use of compositions comprising these nucleic acid molecules would be inherent since they would be required in order to maintain the nucleic acid molecules, plasmids and other vectors, as well as to perform transfections of cells and various assays. An example of a composition comprising nucleic acid molecules and vectors is taught in paragraph 0130 on page 18 (DEAE-dextran).

B. The rejection of claims 1, 7 and 25-28 under 35 USC 102 as being anticipated by NCI/NINDS-CGAP has been withdrawn in view of Applicants' amendments to the claims to recite that the nucleic

acid molecule either comprises SEQ ID NO:12, or encodes a protein at least 99% identical to SEQ ID NO:25. NCI/NINDS-CGAP does not teach these limitations.

8. Claim Rejections - 35 USC § 103

A. The rejection of claims 9-24 and 29-33 under 35 USC 103 has been withdrawn in view of Applicants' amendments to the claims to recite that the nucleic acid molecule either comprises SEQ ID NO:12, or encodes a protein at least 99% identical to SEQ ID NO:25. Neither NCI/NINDS-CGAP nor Sibson et al. teach these nucleic acid molecules, nor do they make obvious any methods of using these nucleic acid molecules.

9. Conclusion

A. No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
August 15, 2003

ROBERT LANDSMAN
PATENT EXAMINER

(1) The genus and the species of the microorganisms recited in claims 18, 20 and 22 should be italicized or underlined.

(2) The objection of claims 10 and 31-33 made on page 3, under item E of the action is incorrect. The examiner states that claims 10 and 31-33 are objected to since they depend from claims rejected under 112, first paragraph regarding enablement. However, claims 10 and 31-33 are rejected under 112/1 for lack of enablement. Further, we do not object claims simply because they depend from rejected claims. We object claims depend from rejected claims only when the objected claims are allowable.